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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/594,990	09/29/2006	Manuel Worcel	0102258.00375US2	4629
24395	7590	04/21/2009		
WILMERHALE/DC 1875 PENNSYLVANIA AVE., NW WASHINGTON, DC 20006			EXAMINER SZNAIDMAN, MARCOS L	
			ART UNIT	PAPER NUMBER
			1612	
			NOTIFICATION DATE	DELIVERY MODE
			04/21/2009	ELECTRONIC

**Please find below and/or attached an Office communication concerning this application or proceeding.**

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

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**Office Action Summary****Application No.**

10/594,990

**Applicant(s)**

WORCEL, MANUEL

**Examiner**

MARCOS SZNAIDMAN

**Art Unit**

1612

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --  
**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

- 1) ☒ Responsive to communication(s) filed on 11 February 2009.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

- 4) ☒ Claim(s) 1, 4 and 5 is/are pending in the application.
- 4a) Of the above claim(s) \_\_\_\_\_ is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 1 and 4-5 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

**Application Papers**

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some \* c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
  2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
  3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

- 1) ☒ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☐ Information Disclosure Statement(s) (PTO/CDC)
- 4) ☐ Interview Summary (PTO-413)
- 5) ☐ Notice of Informal Patent Application
- 6) ☐ Other: \_\_\_\_\_
- Paper No(s)/Mail Date \_\_\_\_\_

### **DETAILED ACTION**

This office action is in response to applicant's reply filed on February 11, 2009.

#### ***Status of Claims***

Cancellation of claims 2-3 and 6-20 and amendment of claims 1 and 4 is acknowledged.

Claims 1 and 4-5 are currently pending and are the subject of this office action.

Claims 1 and 4-5 are currently under examination.

#### ***Priority***

The present application is a 371 of PCT/US05/107384 filed on 03/31/2005, and claims benefit of provisional application No. 60/557,700 filed on 03/31/2004.

#### ***Rejections and/or Objections and Response to Arguments***

Rejections and/or objections not reiterated from previous office actions are hereby withdrawn. The following rejections and/or objections are either reiterated (Maintained Rejections and/or Objections) or newly applied (New Rejections and/or Objections, Necessitated by Amendment or New Rejections and/or Objections not Necessitated by Amendment). They constitute the complete set presently being applied to the instant application.

***Claim Rejections - 35 USC § 103 (new Rejection not Necessitated by Amendment)***

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

The factual inquiries set forth in *Graham v. John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

Claims 1 and 4-5 are rejected under 35 U.S.C. 103(a) as being unpatentable over Stamler et. al. (US 6,472,390) in view of Adams et. al. (US 6,747,063), and over Goodman (US 6,087,398).

Claims 1 and 4-5 recite a method for treating sickle cell anemia or treating thalassemia in a patient in need thereof comprising administering to a patient in need thereof, a therapeutically effective amount of: N-hydroxy-L-arginine, isosorbide dinitrate,

isosorbide mononitrate or a mixture of two or more thereof, and at least one antioxidant (hydrazaline in claim 4 or hydrazaline hydrochloride in claim 5).

For claims 1 and 4-5, Stamler teaches a method of treating sickle cell anemia comprising the administration of an NO (Nitric Oxide) donor (see claims 10, 18 and 21).

Stamler does not teach the use of N-hydroxy-L-arginine, isosorbide dinitrate, isosorbide mononitrate or a mixture of two or more thereof for the treatment of sickle cell anemia. However, Adams teaches that N-hydroxy-L-arginine, isosorbide dinitrate, and isosorbide mononitrate are NO donors (see column 3, lines 43-54).

Neither Stamler nor Adams teach the treatment of sickle cell anemia with antioxidants. However, Goodman teaches the treatment of sickle cell anemia with antioxidants (i.e. reducing agents) (see abstract, claims 1-3).

Since Stamler teaches a method of treating sickle cell anemia with a NO donor, and since Adams teaches that N-hydroxy-L-arginine, isosorbide dinitrate, and isosorbide mononitrate are NO donors, at the time of the invention it would have been *prima facie* obvious for a person of ordinary skill in the art to substitute one functional equivalence (any NO donor) for another (N-hydroxy-L-arginine, isosorbide dinitrate or isosorbide mononitrate) with an expectation of success, since the prior art establishes that both function in similar manner. Similarly, since Goodman teaches a method of treating sickle cell anemia with an antioxidant, and since hydrazaline is a known antioxidant, at the time of the invention it would have been *prima facie* obvious for a person of ordinary skill in the art to substitute one functional equivalence (any

antioxidant for another (hydrazaline) with an expectation of success, since the prior art establishes that both function in similar manner.

At the time of the invention it would have been *prima facie* obvious for a person of ordinary skill in the art to treat sickle cell anemia combining two compositions (any NO donor like N-hydroxy-L-arginine, isosorbide dinitrate or isosorbide mononitrate and any antioxidant like hydrazaline) each of which is taught by the prior art to be useful for the same purpose, in order to form a third composition to be used for the very same purpose. The idea of combining them flows logically from their having been individually taught in the prior art (see MPEP 2144.06). *In re Kerkhoven*, 626 F.2d 846, 850, 205 USPQ 1069, 1072 (CCPA 1980). All this would result in the practice of claims 1 and 4-5 with a reasonable expectation of success.

***Withdrawn Rejections and/or Objections***

***Claims 1-5 rejected under 35 USC § 112, first paragraph (scope of enablement)***

Due to applicant's amendment of claim 1 and cancellation of claims 2-3, the scope of enablement rejection is now moot.

Rejection under 35 USC 112, first paragraph (scope of enablement) for claims 1-5 is withdrawn.

***Claims 2-5, 7-10, 12-15 and 17-20 rejected under 35 USC 112, second paragraph.***

Due to applicant's cancellation of claims 2, 7, 12 and 17 that recited the term "therapeutic agent", the indefiniteness rejection is now moot.

Rejection under 35 USC 112, second paragraph for claims 2-5, 7-10, 12-15 and 17-20 is withdrawn.

***Claims 1-20 rejected under 35 USC 112, second paragraph.***

Due to applicant's amendment of claim 1: addition of the phrase: "to a patient in need thereof", and cancellation of claims 2-3 and 6-20, the indefiniteness rejection is now moot.

Rejection under 35 USC 112, second paragraph for claims 1-20 is withdrawn.

***Claims 1-2 rejected under 35 USC 103 (a)***

Applicant's arguments have been fully considered and are persuasive.

Rejection under 35 USC 103(a) for claims 1-2 is withdrawn.

***Claims 3-5 rejected under 35 USC 103 (a)***

Applicant's arguments have been fully considered and are persuasive.

Rejection under 35 USC 103(a) for claims 3-5 is withdrawn.

***Claims 6-10 rejected under 35 USC 103 (a)***

Due to Applicant's cancellation of claims 6-10 the 103(a) rejection is now moot.

Rejection under 35 USC 103(a) for claims 6-10 is withdrawn.

***Claims 11-15 rejected under 35 USC 103 (a)***

Due to Applicant's cancellation of claims 11-15 the 103(a) rejection is now moot.

Rejection under 35 USC 103(a) for claims 11-15 is withdrawn.

***Claims 16-20 rejected under 35 USC 103 (a)***

Due to Applicant's cancellation of claims 16-20 the 103(a) rejection is now moot.

Rejection under 35 USC 103(a) for claims 16-20 is withdrawn.

***Conclusion***

No claims are allowed.

***Correspondence***

Any inquiry concerning this communication or earlier communications from the examiner should be directed to MARCOS SZNAIDMAN whose telephone number is (571)270-3498. The examiner can normally be reached on Monday through Thursday 8 AM to 6 PM.



If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Frederick F. Krass can be reached on 571 272-0580. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/MARCOS SZNAIDMAN/  
Examiner, Art Unit 1612  
April 11, 2009.

/Brandon J Fetterolf/  
Primary Examiner, Art Unit 1642